REMARKS:

The preceding claim amendments and the following remarks are submitted as a full and complete response to the Office Action issued on February 19, 2009. Figure 1 has been replaced with replacement Figure I in which the recitation of "Reverse Phase-HPLC" in the third box in the diagram is corrected to be "CATION EXCHANGE CHROMATOGRAPHY." This revision is supported by the entire specification and claims, for example, paragraphs [0025]-[0028] and [0037]. The specification is also revised to delete the recitation of "ethanol contained in the concentrate" from paragraph [0037] in Example 3, which was erroneously added. This error is apparent to one skilled in the art from the description of Example 2 because one skilled in the art would readily understand that an IFN-β solution obtained in Example 2 does not include ethanol since the eluent used in Example 2 does not contain ethanol. Claim 4 has been amended to insert the unit "daltons" for "a molecular weight cut-off of 10,000" and to reflect the suggestion by the Patent Office to improve the syntax of claim 4. No new matter has been added. Upon entry of the claim amendments, claims 1-5 are pending. Reconsideration of all outstanding rejections is respectfully requested in view of the foregoing amendment and following remarks.

Objection and Rejection under 35 U.S.C. §112

The Patent Office has suggested amending claim 4 to recite the phrase "with an ultrafiltration membrane with a molecular[1] [weight] cut-off of 10,000," and to specify the appropriate molecular weight units. The Patent Office has also rejected claim 4 under

[1] It appears that the Patent Office inadvertently omits the word "weight" in its proposed language.

35 U.S.C. §112 as indefinite for not reciting any units for a molecular weight cut-off of 10,000. Applicants respectfully submit that since it is common knowledge that the unit of a molecular weight cut-off in ultrafiltration is daltons, one skilled in the art would have readily understood the invention of claim 4 without a need of specifying the unit for "a molecular weight cut-off of 10,000." Nonetheless, considering the Patent Office's suggestion, Applicants have revised claim 4 to recite the phrase "with an ultrafiltration membrane with a molecular weight cut-off of 10,000 daltons," for purposes of additional clarification only. Accordingly, reconsideration and withdrawal of the objection and rejection of claim 4 are respectfully requested.

Claim Rejections under 35 U.S.C. §103(a)

The Patent Office has rejected claims 1-5 under 35 U.S.C. §103(a) as obvious over Carter et al. (U.S. Patent No. 4,483,849) ("Carter") in view of Revel et al. (U.S. Patent No. 4,808,523) ("Revel"), and further in view of Viscomi et al. (U.S. Patent No. 5,244,655) ("Viscomi"). The Patent Office alleges that one skilled in the art would have been motivated to purify IFN-β by practicing a method comprising affinity chromatography using the propylene glycol-containing buffers of Carter or Revel because a skilled artisan would know that IFN-β can be purified by the methods of both Carter and Revel, and that the incorporation of propylene glycol, as taught by both Carter and Revel, would lead to more efficient purification and ultimately a safer therapeutic agent. The Patent Office further asserts that a skilled artisan would also be motivated to incorporate cation exchange chromatography into the methods of Carter and/or Revel because Viscomi teaches this method as effective. Furthermore, the

Patent Office alleges that although neither Carter nor Revel discloses "all of the exact claimed propylene glycol concentration ranges," one skilled in the art would have both the motivation and the ability to optimize the concentration of propylene glycol in the buffers of either Carter or Revel. Applicants respectfully disagree.

As recited in claim 1, the claimed method for purifying human IFN-β comprises washing the column with both a washing buffer solution A and a washing buffer solution B. The two washing buffer solutions A and B are different from each other not only in their concentrations of polyethylene glycol but also in the presence of NaCl as an ingredient. That is, while the washing buffer solution A of pH 6.5-7.5 contains 30-60 wt% of propylene glycol as an essential ingredient, the washing buffer solution B of pH 6.5-7.5 contains 10-30 wt% of propylene glycol and 1-2M of NaCl as ingredients. In addition to these two washing buffer solutions, a buffer solution of pH 6.5-7.5 containing 40-60 wt% of propylene glycol and 1-2M NaCl is used to elute a human IFN-β in claim 1.

While Carter discloses using 40% of propylene glycol as a washing buffer solution for a column loaded with IFN-β, it fails to teach or suggest using additional washing buffer solution containing propylene glycol together with the washing buffer solution disclosed in Carter. Thus, Carter fails to teach or suggest using two different washing buffer solutions in purifying IFN-β.

Revel does not cure this deficiency in the teaching of Carter because the teaching of Revel is limited to use a buffer solution containing 40% of propylene glycol and 1M NaCl for <u>eluting</u> IFN-β. Revel does not even mention using a buffer solution containing propylene glycol for washing the column prior to elution of IFN-β, let alone

teaches or suggests using two washing buffer solutions: a washing buffer solution containing 30-60 wt% of propylene glycol and a washing buffer solution containing 10-30% of propylene glycol and 1-2M NaCl.

Contrary to the Patent Office's position, none of the cited references provides a motivation for one skilled in the art to use two different washing buffer solutions. Although Carter discloses using 40% propylene glycol in 1.0 M NaCl/PO_4 buffer as a washing buffer solution, this disclosure is limited to just a single working example. In contrast, as evident from various disclosures in Carter, the thrust of the teachings and the suggestions of Carter is using a solution of propylene glycol as an eluting solution for IFN-β instead of ethylene glycol See *e.g.*, claim 1; col. 1, lines 35-54; col. 2, lines 29-40; col. 3, lines 54-68; and Example 2. Indeed, Carter consistently teaches 1:1 mixture of 2M NaCl buffered at neutral pH with sodium phosphate and propylene glycol, which is referred to as 50% propylene glycol, for eluting IFN-β from a solid matrix. That is, while Carter teaches using the 50% propylene glycol instead of 60% of ethylene glycol for eluting IFN-β to obtain a higher purification yield, it is completely silent as to whether or how to modify a washing buffer solution in purification of IFN-β except for using a single washing solution containing 40% propylene glycol in 1.0M NaCl. Therefore, Carter fails to provide any motivation for one skilled in the art to modify using propylene glycol as a washing buffer solution such as using two different propylene glycol solutions.

As explained above, Revel lacks any teaching or suggestion of using propylene glycol for washing the column prior to elution of IFN-β. Therefore, one skilled in the art would not have been motivated to use propylene glycol as a washing buffer solution let

alone to use two different propylene glycol solutions as washing buffer solutions.

Viscomi is cited as a reference teaching purification of IFN-β using a method comprising cation exchange chromatography. Viscomi is silent in using any other purification method for IFN—β, let alone using a propylene glycol buffer solution as a washing buffer. Thus, Viscomi also fails to cure the deficiency in the teaching of Carter or Revel.

Applicants respectfully submit that the lack of disclosure regarding using two different propylene glycol solutions as washing buffer solutions cannot be cured under the theory of routine optimization because the missing disclosure is plainly a claim element.

To establish *prima facie* obviousness of a claimed invention, all the claim elements must be taught or suggested by the prior art. See In re Royka, 180 USPQ 580 (CCPA 1974). Since Carter, Revel and Viscomi, alone or in combination, fail to teach or suggest all the elements of claim 1, there is no *prima facie* case of obviousness established, which warrants withdrawal of this obviousness rejection. The remaining claims 2-5 are dependent on claim 1. Thus, claims 2-5 would not have been obvious over Utsumi in view of Carter, and further in view of Revel for the same reason for claim 1.

Accordingly, Applicants respectfully request reconsideration and withdrawal of all the obviousness rejections.

Double Patenting

The Patent Office has provisionally rejected claims 1-5 under non-statutory

obviousness-type double patenting as unpatentable over claims 1-5 of copending Application No. 10/581,602. Since this rejection is provisional, Applicants respectfully request this rejection to be held in abeyance until the present application or the copending application is otherwise indicated as allowable.

In light of the foregoing, Applicants submit that all outstanding rejections have been overcome, and the instant application is in condition for allowance. Thus, Applicants respectfully request early allowance of the instant application. The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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